

Remarks

Claims 121-127 and 129-131 are pending and under consideration in this application. Claims 124-127 and 129-131 are allowed. Claims 121-123 are rejected for alleged lack of enablement and written description. The rejections to these claims are respectfully traversed.

Claim Rejections – 35 USC 112, first paragraph - enablement

Claims 121-123 remain rejected under 35 U.S.C. §112, first paragraph allegedly because “the specification, while is enabling for a full length PRO943 protein of SEQ ID NO: 119, does not reasonably provide enablement for a polypeptide at least 90-99% identical to SEQ ID NO: 119. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims”. For the reasons outlined below, Applicants respectfully disagree.

The Legal Test for Enablement

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure provided by applicants coupled with information known in the art at the time the invention was made, without undue experimentation.^{1,2} Accordingly, the test for enablement is not whether any experimentation is necessary, but whether, if experimentation is required, it is undue.³ The mere fact that an extended period of experimentation is necessary does not make such experimentation undue.^{4,5}

A finding of lack of enablement and a determination that undue experimentation is necessary requires an analysis of a variety of factors (*i.e.*, the *In re* Wands factors). The most important factors that must be considered in this case include: 1) the nature of the invention; 2) the level of one of ordinary skill in the art; 3) guidance provided in the specification, 4) the state of the prior art and 8) the breadth of the claims.

¹ MPEP §2164.0120

² *United States v. Telectronics, Inc.* 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1998).

³ *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

⁴ *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977).

“How a teaching is set forth, by specific example or broad terminology, is not important.”^{6,7} “Limitations and examples in the specification do not generally limit what is covered by the claims ” MPEP § 2164.08. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. The legal standard merely requires that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.⁸

The Disclosure provides sufficient information to enable the claimed invention

Claims 121-123 are directed to a genus of nucleic acid sequences encoding polypeptides which are at least 90-99% identical to the amino acid sequence of the polypeptide of SEQ ID NO:119 and which have a specific and useful function (*i.e.* to a genus of polypeptides that induce chondrocyte redifferentiation).

Applicants respectfully maintain the position that Claims 121-123 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph, for the reasons previously set forth in the Applicants' response filed on January 5, 2005.

As previously stated in the Applicants' response filed on January 5, 2005, Claims 121-123 recite a polypeptide that induce chondrocyte redifferentiation. Therefore, the claimed genus is characterized by a combination of structural and functional features and any person of skill would know how to make and use the invention without undue experimentation based on the general knowledge in the art at the time the invention was made.

⁵ MPEP §2164.06.

⁶ MPEP §2164.08

⁷ *In re Marzocchi*, 439 F. 2d 220, 223-4, 169 USPQ 367, 370 (CCPA 1971)

⁸ *Enzo Biochem., Inc. v. Calgene, Inc.*, 188 F.3d 13 62 (Fed. Circ. 1999), at 1372 (quoting *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991)).

Applicants have provided a nucleic acid sequence of SEQ ID NO:118 and the polypeptide sequence of SEQ ID NO:119. Example 159 of the present application provides step-by-step guidelines and protocols for testing polypeptides that are useful for inducing chondrocyte redifferentiation in mammals. By following the disclosure in the specification, one skilled in the art can easily determine whether a variant PRO943 protein tested positive for inducing chondrocyte redifferentiation in mammals. The specification further describes methods for the determination of percent identity between two amino acid sequences. (See pages 306, line 14 to page 308, line 6). In fact, the specification teaches specific parameters to be associated with the term "percent identity" as applied to the present invention. Accordingly, one of skill in the art could identify whether the variant PRO943 sequence falls within the parameters of the claimed invention. Once such an amino acid sequence has been identified, the specifications sets forth methods for making the amino acid sequences (see page 371, line 6 to page 375, line 21) and methods of preparing the PRO polypeptides. Accordingly, one skilled in the art, given the disclosure in the specification would be able to make the claimed variant amino acid sequences having the claimed biological function. One of ordinary skill in the art had a sufficiently high level of technical competence to identify sequences with at least 90% identity to SEQ ID NO: 119 at the time of filing of the application. Accordingly, one of ordinary skill could practice the claimed invention without undue experimentation.

The Examiner alleges, "...the predictability of which amino acid sequences can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited." (See page 4 of instant Office Action).

Applicants respectfully disagree. Prediction of the variant polypeptide's structure from the sequence is not necessary to practice the instant invention nor is it claimed in the pending claims. Instead, given the specification, one skilled in the art could readily make and identify variants of PRO943 sequence and test them in the "chondrocyte redifferentiation assay" which is well-described in Example 159. This would not require undue experimentation. As discussed above, a considerable amount of experimentation is permissible, if it is merely routine.

For the above-noted reasons, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 USC § 112, first paragraph- written description

Claims 119-123, 130 and 131 are rejected under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. The Examiner asserts that the claims are drawn to polypeptides at least 80-99% identical to SEQ ID NO:119 and thus are genus claims. The Examiner further asserts that the specification does not indicate what distinguishing attributes are shared by the member of the genus. Applicants respectfully traverse this rejection.

The Legal Test for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is "whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." ^{9, 10} The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. ¹¹ The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. ^{12, 13}

In *Environmental Designs, Ltd. v. Union Oil Co.*, ¹⁴, the Federal Circuit held, "Factors that may be considered in determining level of ordinary skill in the art include (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those

⁹ *In re Kaslow*, 707 F.2d 1366, 1374, 212 USPQ 1089, 1096 (Fed. Cir. 1983).

¹⁰ *see also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991)

¹¹ *See, e.g., Vas-Cath*, 935 F.2d at 1563; 19 USPQ2d at 1116.

¹² *Union Oil v. Atlantic Richfield Co.*, 208 F.2d 989, 996 (Fed. Cir. 2000).

¹³ *See also* MPEP §2163 II(A).

¹⁴ 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984).

¹⁵ *See also* MPEP §2141.03.

problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." ¹⁵ Further, the hypothetical 'person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity, have the capability of understanding the scientific and engineering principles applicable to the pertinent art" (Emphasis added).^{16, 17}

The Disclosure Provides Sufficient Written Description for the Claimed Invention

Applicants submit that the instant specification evidences the actual reduction to practice of a full-length PRO943 polypeptide of SEQ ID NO:119, with or without its signal sequence. Thus, the genus of polypeptides with at least 90% sequence identity to SEQ ID NO:119, which possess the functional property of "inducing chondrocyte redifferentiation" would meet the requirement of 35 U.S.C. §112, first paragraph, as providing adequate written description.

Applicants point out that the Specification describes methods for the determination of percent identity between two amino acid sequence (please see the discussion under Enablement). The Specification further describes methods for one of ordinary skill in the art to *identify* peptide sequences having at least 90% identity to SEQ ID NO:119 wherein the polypeptide induces chondrocyte redifferentiation by testing these variants in the chondrocyte redifferentiation assay which is well-described in Example 159, page 530 of the instant specification.

The Office Action alleges that there are no common structural attributes which identify the members of the genus. SEQ ID NO:119 is allegedly insufficient to describe the genus. The Office action asks for a description of the conserved regions which are critical to the structure and function of the genus claimed. There is allegedly no description of the conserved regions or sites at which variability may be tolerated.

Applicants respectfully disagree. Applicants claim those peptides with 90-99% homology to SEQ ID NO: 119 and which induce chondrocyte redifferentiation. As discussed above, and under enablement, one of skill in the art could readily test the variant polypeptide to determine whether it can induce chondrocyte redifferentiation based on the step-by-step methods

¹⁶ *Ex parte Hiyamizu*, 10 USPQ2d 1393, 1394 (Bd. Pat. App. & Inter. 1988).

¹⁷ *See also* MPEP §2141.03.

set forth throughout the specification and in Example 159. There is no need to provide a description of the conserved regions of the polypeptide. Neither is there a need to correlate structure- to- function for the instantly claimed peptides or to identify specific sites at which variability is tolerated. The rejection based on difficulty in structure-function prediction in the art is irrelevant here, since Applicants are not predicting function of variant polypeptides of SEQ ID NO: 119. Instead, as asserted before, Applicants claim those peptides with these prerequisites: 1) 90-99% homology to SEQ ID NO: 119 and 2) which demonstrate a well-defined function, namely, to induce chondrocyte redifferentiation.

Accordingly, the specification provides adequate written description for polypeptides having at least 90% identity to SEQ ID NO:119 wherein the polypeptide can induce chondrocyte redifferentiation. For the above reasons, Applicants respectfully request that the rejection be withdrawn and the claims be allowed.

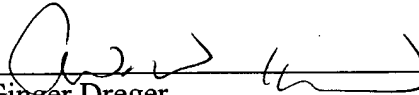
The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C7).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: April 26, 2005


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